EXHIBIT E TO PLAINTIFF'S RESPONSE TO MOTION TO QUASH AND CROSSMOTION TO EXPAND SCOPE OF DISCOVERY

4FI-35

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Food and Drug Administration
Central Region

New Jersey District
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973)
526-6010

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

August 15, 2006

WARNING LETTER

Mr. Divya C. Patel
President
Actavis Totowa, LLC
101 East Main Street
Little Falls, New Jersey 07424-5608 **06-NWJ-15**

Dear Mr. Patel:

An inspection of your firm was conducted by the Food and Drug Administration's New Jersey District from January 10 through February 8, 2006. The inspection was conducted to determine your firm's compliance with the postmarketing Adverse Drug Experience (ADE) reporting requirements of Section 505(k) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 355(k)], and Title 21, Code of Federal Regulations (21 CFR) §§ 310.305, 314.80 and 314.98.

Section 505(k)(1) of the Act [21 U.S.C. § 355(k)(1)] and 21 CFR §§ 314.80 and 314.98 require an applicant to establish and maintain records and to report data relating to clinical experience, along with other data or information, for drugs for which an approved application is in effect. Failure to comply with Section 505(k) is a prohibited act under Section 301(e) of the Act [21 U.S.C. § 331(e)]. 21 CFR § 310.305 further requires manufacturers, packers, and distributors who market prescription drug products that are not the subject of approved drug applications to establish and maintain records and make reports to FDA of serious and unexpected adverse drug experiences.

Deviations demonstrating your firm's failure to comply with 21 CFR §§ 314.80, 314.98[1], and 310.305, which were observed during the inspection, include the following:

[1] 21 CFR § 314.98 requires applicants holding an approved abbreviated new drug application (ANDA) to comply with certain reporting and recordkeeping requirements of 21 CFR § 314.80. Thus, deviations demonstrating your firm's failure to comply with 21 CFR § 314.98 are described in relation to 21 CFR § 314.80.

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1) Failure to submit to the Food and Drug Administration (FDA) ADE reports as required by 21 CFR §§ 314.80(c)(1) and 314.98(a) and 310.305(c). Specifically, there were six potentially serious and unexpected adverse drug events dating back to 1999 for products such as Digoxin, Phentermine, and Phenazopyridine that were not reported to FDA.

   The inspection also found that your firm failed to submit complete and/or accurate information on some 15-day alert reports submitted under §§314.80(c)(1), 314.98(a), and 310.305(c)(1). Examples of information that was omitted from the submitted reports include previous conditions of patients, concomitant medication, event recurrence, and follow-up information obtained from patients' physicians.

   Furthermore, your firm receives published literature on a regular basis, but does not submit to FDA the serious, unexpected cases outlined in the literature as required by 21 CFR 314.80(d) and 314.98(a).

2) Serious and unexpected ADE reports were not promptly investigated as required by 21 CFR § 314.80(c)(1)(ii) and 314.98(a). Specifically, in two cases where the patients' adverse experiences had not resolved when your firm received the initial reports, and in one case where only minimal case information concerning a fatal adverse event had been initially reported to your firm, there were no follow-up investigations.

3) Your firm failed to adequately review ADE information as required by 21 CFR 314.80(b) and 314.98(a). Specifically, data received from all sources, such as spontaneous reports or clinical trials, were not reviewed for seriousness and expectedness. Instead, your firm classified every submitted report as a 15-day alert report.

4) Your firm has never filed a periodic safety report as required by 21 CFR 314.80(c)(2) and 314.98(a). The inspection found that your firm is not following procedures that were established for filing periodic safety reports. This failure to submit periodic safety reports has resulted in at least twenty-six ADEs which were never reported to FDA.

5) Procedures for the surveillance, receipt, evaluation, and reporting of adverse events have not been developed as required by 21 CFR 314.80(b), 314.98(a), and 310.305(a). Specifically, your firm lacks procedures regarding follow-up investigations, adequate completion of the MedWatch form (FDA Form 3500A), maintenance of records to assure timely submission of 15-day reports, and evaluation of adverse event data for serious outcome and event expectedness.

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Neither the list above nor the examples on the Form FDA-483, List of Inspectional Observations, which was issued to you on February 8, 2006, is intended to be an all-inclusive list of deficiencies at your firm, nor a complete listing of late ADE reports. It is your responsibility to ensure adherence to each requirement of the Act and its regulations. The FDA expects drug firms to establish sufficient mechanisms to assure that all ADEs are recorded, evaluated, and submitted to the FDA within established time frames as outlined under 21 CFR §§ 310.305, 314.98 and 314.80.

The specific violations noted in this letter are serious and may be symptomatic of underlying problems. You are responsible for investigating and determining the causes of the violations identified above and preventing recurrence of similar violations.

We have received your February 28, 2006 response to the Form FDA-483, and have made it part of our official files. Your response does not include details that were discussed during the inspection. Specifically, you indicated in discussions during the inspection that ADE reporting would be handled by Alpharma because a well-established system already exists at that site, and Alpharma is owned by Actavis, which is your parent firm. The written response does not state this, nor does it include an explanation of how reports received by Amide will be transferred to Alpharma for review and reporting. Documents provided to the investigator during the inspection appear to be for an Actavis Medical Affairs/Drug Safety Group based in Piscataway, NJ, not Alpharma in Elizabeth, NJ. Please clarify reporting responsibilities, actual location of the medical affairs group, transfer logistics, and applicable Alpharma or Actavis procedures.

In addition, your response does not identify the cause of the observed deficiencies with regard to postmarketing reporting requirements. Several of the observed deficiencies were long-standing, and there is no indication of how or why the lack of compliance was not identified by your firm, and why it was allowed to continue for such an extended period of time. Does your firm have any insight into this situation, and are you reviewing all other regulatory requirements applicable to your firm to assure that you are in compliance with those requirements?

Based on our observations during the inspection and information submitted by your firm to comply with the drug listing requirements of Section 510(j) of the Act [21 U.S.C. § 360], your firm manufactures numerous prescription drug products without approved applications. These include buspirone HCl tablets (5, 10, and 15 mg); carbetapentane tannate and chlorpheniramine tannate tablets (60 mg/5mg); guaifenesin and pseudoephedrine HCl extended release tablets (1200 mg/120 mg); hyoscyamine sulfate tablets (0.125 mg); Nicomide tablets; and yohimbine HCl tablets (5.4 mg). These products appear to be unapproved new drugs introduced into interstate commerce in violation of section 505(a) of the Act [21 U.S.C. § 355(a)]. This is not intended to be an all-inclusive list of your firm's

drugs that are marketed in violation of the drug approval requirements. We request that, within fifteen working days of receipt of this letter, you provide us with a list of all drugs that you manufacture or market, along with, for each drug, the NDA or ANDA number under which you manufacture or market the drug or a statement describing the basis on which you claim for the drug an exemption from the drug approval requirements. For each drug marketed without an approved application, please also provide the labeling for the drug product.

You should take prompt action to correct all of the deficiencies discussed above. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions may include, but are not limited to, seizure of your products and/or injunction. Federal agencies are advised of the issuance of all Warning Letters relating to drug products so that they may take this information into account when considering the award of contracts.

We request that you reply in writing within fifteen working days of receipt of this letter regarding our questions about your initial responses. If corrective actions cannot be completed within fifteen working days, please state the reason for the delay and the timeframe within which corrective actions will be complete.

Your response should be directed to: U.S. Food and Drug Administration, 10 Waterview Boulevard, 3rd Floor, Parsippany, New Jersey 07054, Attn: Sarah A. Della Fave, Compliance Officer.

Sincerely,

Douglas I. Ellsworth
District Director
New Jersey District

cc: Mr. Sigurdur Olafsson
President
Actavis, U.S. Operations
990 Riverview Drive
Totowa, New Jersey 07512